VOLUME XIII August 1957 NUMBER 8

Clinical Proceedings

OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

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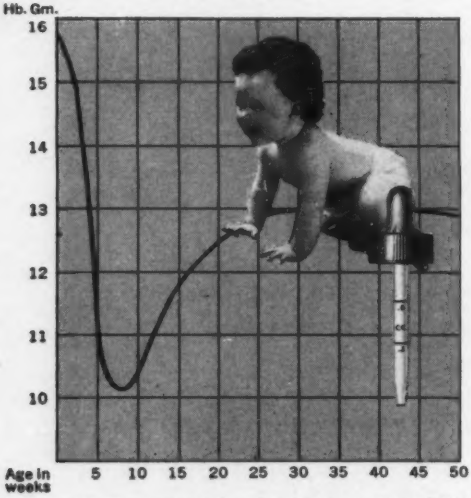

Chart adapted from Niccum, Jackson and Stearns: A.M.A. Am. J. Dis. Child. 86: 553, 1953.

Mean hemoglobin determinations of infants on a predominantly milk diet receiving Fer-In-Sol. The Fer-In-Sol dose was 5 mg. of iron (0.2 cc.) per day at 3 months, increased to 10 mg. of iron (0.4 cc.) after 6 months of age.[1]

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(1) Niccum, W. L.; Jackson, R. L., and Stearns, G.: A.M.A. Am. J. Dis. Child. 86: 553, 1953. (2) Smith, C. H.: Bull. New York Acad. Med. 30: 183, 1954. (3) Smith, N. J., and Rosello, S.: J. Clin. Nutrition 1: 375, 1953. (4) Sturgeon, P.: Pediatrics 13: 107, 1954.

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JUVENILE SCHIZOPHRENIA

Reginald S. Lourie, M.D.,* Earle Silber, M.D.,† Jonathan Williams, M.D.,‡ Mary Robinson, M.A.,§ Carlos Berrocal, M.D.‖

This case is presented to illustrate the dilemma with which one is often faced in determining the role of brain damage in the production of a schizophrenic-type picture. Perhaps one should think more of the schizophrenic reaction in the child as being a symptom, or as being a response to a set of conditions which he either temporarily or permanently cannot handle.

CASE REPORT

J. W., a three-year-old negro boy was admitted to Children's Hospital in October 1956 for study of grossly abnormal behavior, considered possibly schizophrenic in type.

The patient was the product of a full term uncomplicated pregnancy. The pregnancy, although unplanned, was desired since the only other male sibling was not fathered by the mother's present husband. There were no feeding or sleeping difficulties. The infant sat up at 6 months of age, crawled at 7 months, and walked at 15 months. He began feeding himself at 3 years of age. At one year of age the mother attempted bowel training. Such training was resisted by the child who, when he defecated in his diaper after removal from the "potty", would be spanked by the irritated mother.

The mother noted that the child had "always wanted to be babied" and she did baby him until the birth of the next sibling. In the past, the child had always wanted to be picked up but recently had ceased this demand. He often rocked himself on his hands and knees and banged his head on furniture. The mother believed that the child "has never acted in a normal way". Although he mumbled, he had never developed coherent speech, but would point to desired objects. He had frequent severe temper tantrums precipitated by no obvious cause, and fought vigorously with other children, biting, scratching, kicking, and screaming. He entered into games with the other children, but played only long enough to obtain a desired object. Then he would play alone. During the year prior to admission, the mother was concerned by the child's handling of his genitals, but considered him "to be pacifying himself". She thought his genitals to be "a terrible size, as big as the eight-year old child's".

The mother had come from a broken home and had frequent crying spells until she was eleven years of age. She showed considerable resentment in noting that she had always fought her brother's battles in school. The patient's father was described as a "good provider", his wife's only complaint being that he went out at night with his

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friends a great deal. Until twelve years of age he had had "falling out" spells which ceased following a circumcision operation. The patient's siblings included an older half brother who was described as slow in development and nervous. Two female siblings were described as average and "did not have to be trained". The youngest was said to have had "falling out" spells.

On admission to the hospital, the patient was noted to be a small, frail, negro boy who was withdrawn and suspicious. He lacked the coordination of movement typical for a child of his age. He walked in a crouched position with his head tilted to one side. There were, however, no abnormalities noted on either general physical examination or complete neurological examination. When first admitted to the hospital, he had to be kept in bed because he was playfully destructive. At night he required sedation to prevent screaming which disturbed the other children. At meals he appeared animal-like and fed himself with his hands. He consistently ignored other children and only transiently desired the attention of adults.

Laboratory studies during hospitalization included a normal hemogram, urinalysis, and cerebrospinal fluid examination. Electroencephalograms on two occasions demonstrated an abnormal pattern with bilateral temporoparietal foci, more marked on the left. A pneumoencephalogram was unsatisfactory. The right ventricle was poorly visualized and the left not at all.

During the period of hospitalization there was some improvement in behavior. The child became more friendly and seemed to be interested in both fellow patients and personnel. He appeared to be happy and wanted to be held when his mother visited him. There was, however, no change of mood when she left. He became less greedy at the table but still fed himself with his hands. He continued to defecate in bed, but did not play with the feces. At his initial play interview he refused to participate in any activity with the interviewer. He was withdrawn and fought if approached. At later sessions he became more cheerful but played with a very short attention span.

Mrs. Robinson:

When I first saw the patient in the clinic waiting room and suggested he come with me, he clung to his mother and merely whimpered silently. At this point we decided that it might be best if the mother accompanied him as far as my office. Although he showed no hesitancy at all on getting into the elevator, as soon as the elevator began to ascend he became quite terrified, clutched at his genitals, and again threw himself at his mother, whimpering.

When we arrived at my office he was reluctant to have his mother leave, but still there was no speech. When she did leave he ran to the door and began pawing at it. He next sat on the floor, clutching at his genitals and began to rock back and forth in a rhythmic fashion, while making humming sounds to himself. There were a few speech sounds, but these were merely isolated syllables. He next started laughing, and then began an alternate laughing and crying behavior which could not be related to the external situation. He was also very fond of going to the corner of the room, kneeling and rocking, facing toward the corner.

The quality of his coordination varied quite widely during the examination. He was consistently awkward and incoordinated in the use of his

hands. At times he walked upright with only a slight inversion of his feet. However, at other times he walked in a bent over position, flexed at the waist and knees, with head inclined to one side and his hands held up in front of him. When seating himself he would rotate and settle down much as animals settle to lie down.

He was completely unrelated to me throughout the examination and seemed so oblivious to what was going on that I questioned his hearing. However, when I dropped a book on the floor behind him, there was a distinct startle response although he did not turn around toward the source of the noise. He was completely unrelated to any object in the environment with the exception of a doll to which he became quite attached and clung. Several times, he dashed the doll to the floor, picked it up, and then continued to dash it to the floor and pick it up again. He got quite a bit of pleasure out of this activity.

Due to his lack of relatedness and apparent inability to understand either oral or pantomime directions it was quite difficult to administer any standard test. I was eventually able to give him portions of the Gesell Scale of Infant Intelligence. On the basis of this, I estimated his general developmental level to be around 17 months, with his motor and social behavior being closer to 18 or 19 months, and his language and adaptive behavior in the 15 month range. Since I had been unable to test the child adequately I interviewed the mother after I had seen him and asked her about his activities, using a Vineland Scale of Social Maturity as reference. On this basis he had a social age of 19 months, although this may represent some exaggeration on the mother's part. It was quite interesting that she stated his only understandable speech was "stop that" which he apparently does say quite clearly. She did feel, however, that he could understand a great deal asked of him and was capable of obeying quite complicated directions. She illustrated this by saying, "I can ask him to go upstairs and get the strap, and he will get it. However, I usually use it for my baby boy, who is the one who is bad". In responding to my questions she gave me the impression of being a rather passive, yet extremely hostile person, who characterized her relationship with the boy by saying, "He always seemed to be going backwards, ever since he was born".

It is, of course, quite difficult to make a differential diagnosis in such a case because there are certain aspects of this child's behavior pattern that are compatible with brain injury, and others with juvenile schizophrenia. His motor pattern is disturbed and his postural righting mechanism seems somewhat defective. However, this disturbance in the motor pattern with the unusual gross postural position was not consistent since he walked upright for a long period of time and then suddenly, for no apparent reason, bent over and began to exhibit this strange behavior.

The fact that he is very distractible in one sense is compatible with a

diagnosis of brain injury. However, he is not distracted by objects in the external environment which is what we most often find. In this case, we cannot relate the child to his external environment at all. He seems much more distracted by his own ideas or thoughts. I think that we might assume that this is a child whose perception of reality is very poor on an organic basis, and who has shown a schizophrenic adaptation since reality has so little meaning for him.

Dr. Silber:

After this child had been studied on an out patient basis we still felt that we could not be sure of the diagnosis, and for this reason arranged for further study in the hospital.

One question we wished to answer was: How much was his capacity for relating to people seriously impaired, or how much out of contact with reality was he? Would it be possible that exposure to people in the hospital would result in increase in ability to relate? It was the feeling of the people who observed him in the clinic that it was not possible to reach him. He was described as being more like an animal than a child. We further wished to investigate what neurological problem might also be involved in explaining his behavior. I think there has been a very significant change noted in this child since he has been in the hospital. He now seems to have the capacity at least to perceive people and to respond to someone like Dr. Berracol with whom he has been able to establish a relationship. It is true that he still has serious difficulty in this area, but I no longer have the impression of him as a child who is impossible to reach and who really finds contact with people so painful that it is necessary for him to shut himself off defensively from relationships.

Dr. Lauretta Bender considers childhood schizophrenia to be a problem of a general maturational lag, and feels that failure of development involves not only psychological areas, but also a general immaturity in the development of the whole nervous system which includes retention of primitive posturing reflexes. For example, she feels that she can demonstrate continued whirling in schizophrenic children who are rotated. I do not think that this child demonstrates this phenomenon.

It is my impression that what we are dealing with in this case is a combination of organic factors coupled with serious psychological problems involving relationship with the mother. I do not feel that his relationship disturbance is so severe and fixed that it would justify a diagnosis of childhood schizophrenia.

One of the problems in diagnosing childhood schizophrenia is that the term is frequently used to mean different things to different psychiatrists. For example, Dr. Bender would consider some of these disturbed neurological patterns to be consistent with the diagnosis. She described

what she believes are three varieties of this condition. The first is the autistic or pseudo-defective type which is illustrated in a child who appears quite withdrawn, uninterested in people, is frequently thought to be mentally defective or perhaps deaf, and who in general is not responding to his environment. The second type she describes is a pseudo-neurotic form in which the child has severe phobias, obsessional symptoms, compulsive patterning, and a whole variety of psychoneurotic manifestations of such severity as to be really quite crippling. She also describes a third type a pseudo-psychopathic variety in which the child has a good deal of difficulty with impulse control and is consequently involved in psychopathic acting out episodes but where the basic problem is schizophrenia.

Leo Kanner describes infantile autism which he feels is not synonymous with childhood schizophrenia although the terms are often used interchangeably. According to Kanner infantile autism is manifested in the inability of a child to relate even in the first year of life, and in addition, a failure of language development. These children become fascinated with objects rather than people and are very disturbed if there are any changes in routines in the environment. Kanner also makes the point that these children have good cognitive potentialities. I do not think this child precisely meets Kanner's definition of infantile autism.

Other people have thought of childhood schizophrenia as being predominantly and essentially a psychological phenomenon. Margaret Mahler describes two varieties. The first she calls the symbiotic type, where the mother and child are so involved with each other that the child cannot separate from the mother, and relate to anyone else. There is a real disturbance in the child's ability to develop any concept of himself as a separate person from his mother. The second type she calls the autistic variety where the child seems never to have related even to his mother. Other workers such as Bruno Bettelheim consider schizophrenia as an adjustive or psychological process in which the child is responding to really life threatening stress in relationship to significant figures in his environment. Szurek operates on the assumption that schizophrenia can be understood solely in terms of disturbances of relationship within the family.

To return to this child, I feel that we are dealing with a combination of organicity and relationship disturbance. Although I feel there is some serious question of the possibility of childhood schizophrenia, I do not feel, on the basis of observations that have been made on this child's increasing capacity for relatedness, that such a diagnosis is warranted.

Dr. Lourie:

The child who is ordinarily thought of as schizophrenic is actually presenting no different a picture than the usual normal two-year-old who is brought into the hospital. For the first 24 or 48 hours such a child may be

unrelated, and regressed. If this normal child who within 24 hours will recover completely and be quite well related is seen in the middle of this withdrawal period, he may look very much like the schizophrenic child. So we do see schizophrenic-like patterns on a transitory basis. We also hear of very severe schizophrenic reactions that clear up in a week, or a month, or a year. In other words, the more variety we see in the symptom pattern the more we can be convinced that there may be a variety of situations and etiologies capable of bringing about this type of personality response.

It has been thought in the past that the predominant reason for a child's developing this severe type of personality withdrawal was purely and simply a disturbance in the relationships in the family: the mother-child relationship or perhaps the father-child relationship. As a matter of fact we find in the literature that mothers whose type of handling tends to produce schizophrenia in their children are known as "schizophrenogenic" mothers. In this type the mother makes such complete demands on her child (even her infant has to supply certain kinds of satisfactions for her) that the situation soon becomes intolerable to the child and he withdraws or remains in this very early infantile symbiotic state that Dr. Silber described.

This certainly does not cover all the varieties of withdrawal reactions and unrelatedness we see in children, and more and more we have become aware that there is a very large constitutional element. The more we come to know about very small infants the more we realize that there is a great variety of possible responses. There are forms of minor brain damage that lead to unusual sensitivities. One such sensitivity that I am sure the pediatrician has seen in his practice is an intolerance for noise or an extreme sensitivity to touch. The mother says, "This is a child I have never been able to get close to". The child was withdrawn right from birth and would be very unhappy if anyone tried to get close to it. The tendency is often to blame the over-demanding "schizophrenogenic" mother or rejecting mother. Since the mothers of these children read they may read of this type of indictment which certainly does not always hold. Many mothers of such children, as a result of their reading, feel very guilty about their role in the creation of this pattern in their infants. Considerable maternal anxiety is frequently a concomitant of the schizophrenic picture in the child, but it must be determined which came first.

I think it is very important for us to scrutinize just what kind of child we have, and determine what kind of nervous system he has, what kind of occult damage has occurred, or what kind of developmental delay there is which makes it so difficult for the child to relate to his mother, rather than the other way around. The more children we save at birth who would formerly have died, the more children we will rear who are carrying these minor brain defects, these minor neurological distortions into their later

lives. In one sense the children with more severe neurological damage are more fortunate since they are easier to diagnose and there are facilities to take care of them. There is this increasing group in which we have few clinical diagnostic approaches that will pinpoint where the difficulty lies. The best we can say is that there are subtle signs of disturbance. We might suspect that they are aphasia-like. By the same token they are not anything like the classical aphasias one sees in adults or in children who have brain damage later in childhood, whether on an infectious or traumatic basis. These children may have vague distortions, inability to distinguish distance and space, that is, visual-motor disturbances. They may not have any hearing difficulties, but instead have difficulty in integrating what they hear into meaning. We see such children with these minor defects trying to understand the world by bringing their still intact senses to bear to make up for those which have been damaged. One child I have recently seen demonstrated this very well. He put anything new into his mouth, smelled it, and rolled it in his fingers. He had to bring everything into his pattern of experimentation where the intact senses could take over to try to make up what in this child was a more obvious type of auditory aphasia. Although he heard perfectly well, he could not understand what was told him, but he could understand what was shown him.

Such children while growing up have different needs. The timetable of personality development in children with these mild organic handicaps is different as are their needs from their mothers. Of course, when you have a child with these special needs it becomes less likely that he will receive the kind of handling that will meet these needs, whereas his normal siblings brought up in the same environment without these special needs from their mother will be able to develop perfectly normally. As a result more of these mildly affected children tend to turn away and develop autistic patterns. Varying with the intensity and duration these patterns may or may not be reversible.

I think we are just beginning to be able to pinpoint a little more definitively the problem of what childhood schizophrenia is. The more we have to deal with it the more we begin to see the organic roots and the more we become convinced that it is not an "either/or" problem. Incidentally more and more we tend to rely on the psychologist for the diagnosis of these minor occult kinds of neurological disturbances which still have the power to influence a child to such an extreme degree. It is in the psychological tests that we find the greatest ability to pick up these minor distortions.

We still have not matched our increased diagnostic facilities with facilities for doing anything about these children. Most of these children, if nothing is done, will end up in institutions for the defective unless we think more in terms of specific remedial approaches.

Dr. Williams:

It has been my lot over the past ten years to see a large number of children variously regarded as retarded, autistic, or schizophrenic, and to pass upon the integrity of their nervous systems prior to a psychiatric decision as to what to do for the child. I have been impressed by one thing. I do not believe I have ever seen a child so characterized who did not have an abnormal electroencephalogram. This is not true of schizophrenia as we know it in the adult though frequently there has been some electroencephalographic disturbance of varying degrees yet not with the constancy that we see in autistic or schizophrenic children.

In this particular child I was interested in examining the history. We find what might be referred to as a "positive" family history of seizures. The father had seizures, and an aunt, and uncle, I believe, had a history suspicious of seizures. In particular, this child has an abnormal electroencephalogram with findings especially localized to the temporo-parietal regions, more marked on the left. We know that certain paroxysmal behavior disorders have a definite organic origin. Psychomotor seizures tend to have their foci of abnormal activity within the temporal lobes, and in older children and adults it is recognized that the temporal lobes play more than a little part in the total behavior pattern of the individual. Working on the statistical assumption that this child is probably right-handed we can consider that his dominant cerebral hemisphere is on the left side, the side which seems to show the greater predominance of abnormality. Within this dominant hemisphere lie those areas of special activity regulating the symbolic meaning of the certain sounds and sights of which Dr. Lourie spoke. Damage to this region could possibly result in receptive or expressive aphasia. I would agree with Dr. Lourie that there is much more than a passing coincidence between evidence of organic disease in a child whose behavior is such that it might be considered childhood schizophrenia.

THE THERAPY OF DIABETIC COMA

Discussed by: Thomas E. Cone, Jr., Capt., MC., USN*
Case presented by: Gloria Eng, M.D.†

The duration of diabetic coma with its concomitant decrease in cerebral oxygen uptake is definitely related to increasing mortality. It is therefore imperative to institute vigorous therapy to combat this serious complication of diabetes mellitus as promptly as possible.

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CASE PRESENTATION

M. D., a twelve-year-old negro girl was admitted to Children's Hospital on July 5, 1956 with diabetic acidosis; she had a blood sugar level of 450 mg. per 100 ml., and CO_2 combining power of 9 volumes per 100 ml. She was known to be diabetic for the five previous years, and had been receiving 20 units of protamine zinc insulin (PZI) and 10 units of regular insulin daily. While visiting here in the city she indulged in dietary indiscretions and variations in administration of insulin. Two days prior to admission she noted generalized weakness, loss of appetite, and craved water but not food. The day prior to admission, she took only a minimal amount of food, complained of right shoulder pain followed by right abdominal pain, and began to breathe deeply.

On admission, physical examination revealed an apprehensive, disoriented twelve-year-old girl, screaming for water and breathing deeply 40 times per minute. Her blood pressure was 120/80, pulse rate 124 per minute, and rectal temperature was 100.2°F. Except for moderate dehydration and a sweet "fruity" odor to her breath there was no other evidence of abnormality. Parenteral fluid therapy was started immediately. Initially she was given normal saline, followed by a "homeolyte" solution and a 1.4 per cent solution of sodium bicarbonate to correct this carbon dioxide combining power deficit to half-normal levels; she also received regular insulin by subcutaneous and intravenous routes. Acidosis was gradually eliminated except for a lapse on the second day of hospitalization. She was soon given oral feedings, and regular insulin in four daily doses, as well as procaine penicillin in a daily dose of 600,000 units for prophylaxis. The total available glucose and glucose insulin ratio were determined, and the patient was discharged on a diet containing 200 gm. of carbohydrate, 90 gm. of protein, and 90 gm. of fat, and was to be followed in diabetic clinic. She was also to take insulin as follows: 24 units of PZI and 12 units of regular insulin before breakfast, 8 units of regular insulin before lunch, and 8 units of regular insulin before supper.

Capt. Cone:

Children in diabetic coma are hyperglycemic, dehydrated, and acidotic. Most have lost approximately 10 to 15 per cent of their body weight; this amount of water and electrolyte loss gives rise to severe dehydration. They are not eating, and starvation ketosis is added to the already serious metabolic imbalance. Tissue cell breakdown results in greater intracellular than extracellular loss of water. The extracellular losses are not quite so great because the high osmotic pressure of this fluid tends to deplete the cells of water.

What is the best way of treating these children? On this point many disagreements may arise, but in general, proper treatment concerns itself with establishing a routine which is satisfactory to the individual hospital and then sticking to it so long as it is physiologically reasonable.

Hyperglycemia requires insulin. The feeling throughout the country towards insulin has changed within the last ten years. Formerly, much larger initial doses of insulin were given. A satisfactory initial dose of insulin is now generally considered to be two units per kilogram of body weight. This is our routine. If the child is stuporous or comatose, as was the child

under discussion, we would administer 75 per cent of the total amount subcutaneously and the remainder intravenously immediately following admission to the hospital. We follow this by the administration of intravenous fluids. In our hands, gastric lavage is an important adjunct in therapy since we have found that the vomiting which is a very frequent symptom in diabetic acidosis is often decreased by lavaging the stomach.

With particular reference to fluid therapy we usually start with a hypotonic solution of from one-third to one-half normal saline, and continue this solution until the patient begins voiding. We do not use any sugar containing solution in the early phase of treatment. Since these children have lost 10 to 15 per cent of their body weight we consider them severely dehydrated. If one relates this to surface area approximately 3,000 milliliters of total fluid per square meter of body surface is needed during the first 24 hours.

Initially we withdraw blood for determination of serum electrolytes, although this is not strictly necessary since we can pretty well estimate what the electrolyte pattern will be. The laboratory finding we are mainly interested in, however, is the level of blood glucose. After an hour of insulin and fluid therapy we obtain another blood glucose level, and if necessary give additional insulin.

After the child begins to void satisfactorily we change from our initial hypotonic saline solution to a multiple electrolyte solution. We continue to use a glucose free solution for the first three or four hours of treatment. There is no doubt that these children need sugar. Liver and muscle glycogen is severely depleted and, in the absence of adequate insulin cannot be redeposited. Insulin, of course, tends to correct this condition and facilitates redeposition of glycogen, but early in the course of therapy, before insulin has had time to act, administration of sugar solutions will merely cause a sugar diuresis with further loss of solutes in the urine. After the first three to four hours of therapy we substitute a balanced electrolyte solution containing 5 per cent glucose or fructose. Some people feel that fructose metabolism is less disturbed in the presence of severe acidosis and should therefore be employed.

Our balanced electrolyte solution will, of course, contain potassium which is a controversial ion as you know. Several workers in this field have described successful clinical results during the first day of therapy, using only normal saline without any added potassium. They are impressed by the absence of any clinical signs of potassium deficit. They do, however, administer potassium to these patients 24 hours later. We feel, however, that potassium is vitally necessary. The use of potassium in the diabetic patient in acidosis makes a great deal of sense physiologically. For one thing these patients are under increased stress, their corticosteriods are elevated, and

their corticotropin activity has increased; this would increase loss of potassium in the urine prior even to the onset of the acidosis and coma. In addition, as these patients are treated the extracellular fluid re-expands rather rapidly, and there is a dilution of potassium in the extracellular space. Then too, as glucose is administered, cellular glycogen is formed and redeposited, and potassium is carried back into the cell. In view of these factors, all of which are operating almost simultaneously we feel that potassium greatly improves the general clinical condition of these children because it is one of the essential elements for normal cellular function. We see no reason at all why it should not be given especially if glucose is being given. Of course, we do not use solutions containing potassium if the child does not have a satisfactory urinary output.

The presence of a normal serum potassium level at the onset of the illness does not mean very much. Potassium, therefore, in my opinion is very necessary, so much so that if one gives a glucose containing solution and insulin without potassium, one can throw these children into an acute potassium deficiency with resultant respiratory paralysis. We use routinely between 20 and 30 milliequivalents of potassium per liter of balanced electrolyte solution.

I would like to comment about our use of lactate in preference to bicarbonate in correcting the acidosis. We very infrequently find it necessary to use bicarbonate. Instead, we use a solution containing 20 milliequivalents of lactate per liter. In our experience we have noted a relatively short lapse of time, approximately 2 hours, before our children are brought out of coma. In a few cases we found the return of the pH levels of the serum to 7.35 and even 7.38 during this period. I have always been impressed by the admonition given in textbooks in referring to the use of $\frac{1}{6}$ molar lactate to correct acidosis. A method is described for calculating the amount of lactate needed to raise the carbon dioxide combining power to the desired level; half the calculated amount is then recommended to be administered immediately.

Perhaps the fact that we see only a very few severely comatose children is an important reason for our not using bicarbonate. Our patients are usually under regular medical surveillance and at the very onset of drowsiness or stupor we refer them to our hospital. We do not see children who have already been in moderate coma for several hours, and who are then brought to us in deep coma. In such a case I think probably the use of bicarbonates or other alkalies would have a definite place, because, as Kety's work has shown, in profound acidosis there is marked decrease of oxygen uptake by the brain. Therefore, time would seem to be of the essence in shifting the child from an acidotic to a normal blood pH.

Differences of opinion exist on how much insulin to use. I think that it

all depends on the duration of the acidosis and whether the insulin is given intravenously or subcutaneously. As you know, these children are so dehydrated that they may be in shock, and insulin may not be picked up from subcutaneous depots. It is most important, therefore, to give some insulin intravenously. Furthermore, I can see no harm in giving large initial doses of insulin. Even if one gives too much and causes a profound hypoglycemia it is very simple to correct this by giving 10 per cent glucose or 50 per cent glucose intravenously.

Now, for the post acidotic glycemic equilibrium we have been tempted to follow Brush's[1] method of initial stabilization. This is a mechanistic way of treating diabetes, and it is very simple. The basic physiologic principle is to give more insulin than the child actually needs, thus putting the Isles of Langerhans at rest. After a few weeks the diabetic child will begin secreting enough endogenous insulin to maintain quite a satisfactory metabolic balance. The amount of protein, carbohydrate, and fat is very precisely spelled out, and the amount of regular insulin to be given four times a day is also outlined. Within a week these children begin going into insulin shock and the insulin dose is lowered. Frequently, after starting with 50 or 60 units, at the end of three weeks one might be giving as little as two, three, or four units of insulin. This is very helpful because even though such a low dose of insulin will not be maintained the parents will have between six weeks and three months of administering just one small dose of regular insulin daily. By that time one has been able to lay the groundwork for psychologic care, adjustment of diet, and discussion with the parents on how to prepare the child to give himself his own injections.

There are many other ways of stabilizing a child. Perhaps the most popular and the most generally used throughout our country is the Hartmann method of the so-called "G/I or glucose/insulin ratio". This is calculated by first giving the child a typical American diet in which approximately 15 per cent of the calories are derived from protein, about 35 per cent from carbohydrate, and 50 per cent from fat. This can also be worked out in grams per pound of body weight by giving about three grams of carbohydrate, one of protein, and one and one-half of fat per pound of body weight which makes a total caloric intake of approximately 29 calories per pound of body weight. A child with one square meter of body surface and weighing approximately 60 pounds would receive about 180 grams of carbohydrate, 60 of protein, and 90 of fat when placed on this regime. Then, on the basis of fractional urines the required amount of regular insulin is determined. For example, our 60 pound child on a balanced diet with 180 grams of carbohydrates might be receiving forty units of insulin. The next thing we do is to ascertain the total available glucose, or T.A.G., in 180 grams of carbohydrate. To do this we measure the total amount of glucose

in a 24 hour urine specimun, and subtract that from the glucose of the diet; this gives us the amount of glucose actually metabolized by the body. We then divide that difference by the number of units of insulin given in a 24 hour period. This gives us our G/I ratio. To illustrate, let us take this child with 180 grams of total available glucose. If he is putting out 20 grams of sugar in his 24 hour specimen of urine he is actually metabolizing 160 grams. If we are giving him 40 units of insulin his ratio would be 4:1; that is for each unit of insulin given he has metabolized 4 grams of carbohydrate.

The next question which logically arises is whether to use regular, long acting, or a mixture of the two types of insulins. We start out in our patients by using regular insulin, and for the first few days give about 40 per cent of the total dose before breakfast, 20 per cent before lunch, 30 per cent before supper, and 10 per cent at midnight. Then when the G/I ratio rises as the endogenous supply of insulin returns and the child is better able to handle his diabetes we stop the midnight dose, and give 50 per cent before breakfast, 20 per cent before lunch, and 30 per cent before supper.

After a week or so the child's urine is usually free of acetone, and contains perhaps one plus sugar occasionally; he is doing well, eating well, and looking well. Now we would change to N.P.H. insulin which as you know is actually a mixture of two units of regular for each unit of protamine zinc insulin. Its maximum effect if one gives it before breakfast occurs sometime late in the afternoon. We use the same total number of units of insulin as we have worked out with the G/I ratio, giving 80 per cent as N.P.H. in the morning and 20 per cent as regular about 4 o'clock to control the child following the evening meal. The only thing we insist on is that the child remain on a rather fixed daily amount of carbohydrate so that we have a stable point of reference.

The long-range handling of the diabetic, the growth, development, and psychologic aspects of diabetes in the child, and also the effect that the child's diabetes has on the parents cannot be considered in such a short time, although they are very interesting and important topics.

Question:

Do you calculate the percentage of fat and protein which is presumably converted to carbohydrates in the total available glucose?

Capt. Cone:

No, because when we start using the G/I ratio we presume that the child is receiving sufficient insulin, is no longer acidotic, is not showing marked ketosis, and is therefore not really utilizing much of his protein and fat for glucose. We give the parents a substiution list which allows the children to stay within the ratio and yet, for example, eat a piece of cake occasionally. The parent-child-doctor relationship becomes a very difficult one for the

long haul especially in the case of an adolescent diabetic. Not only is the adolescent diabetic rebelling against the world, his parents, and the doctor, but he is also rebelling against his diabetes. He must keep up with his crowd and be part of the gang; he must have the cola or sandwich or milkshake that the rest of the gang has. One might expect the two to five year olds who are so sporadic in their eating to present a special problem and frequently they do. However, I have been amazed at how little trouble we have had with the little diabetic children; they seem to have pretty good appetites. We have tried to impress on the parents the necessity of exercise, fresh air, and not too much concern. We usually give them Aldrich's book, "Feeding Our Old Fashioned Children", and discuss the problems of feeding with them at some length.

Question:

Have you had occasion to use "oral insulin"?

Capt. Cone:

No, but a physician who was formerly associated with me a few years ago is now a member of the medical staff of a pharmaceutical company manufacturing one of these substances, and his information relating to oral hypoglycemic drugs is that in the small series with which he was acquainted they were not very effective in children. They are anti-insulinase substances, and the problem in children is actually deficiency in the quantitative or qualitative amount of insulin rather than any variation in insulinase activity. Therefore, it probably will not play a big role in pediatric practice.

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BILATERAL PAROTID GLAND ABSCESS IN A NEWBORN INFANT

Sydney Ross, M.D.*, Grace H. Guin, M.D.†, Caroline Jackson, M.D.‡

Resuscitation procedures at birth may in themselves play an important part in the pathogenesis of neonatal infection. This is illustrated in a fatal case of a parotid gland infection in a newborn premature infant, in which *Staphylococcus* was the etiologic agent.

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CLINICAL SUMMARY

P. M., a 5 day old negro female infant was transferred to the Children's Hospital of the District of Columbia from the hospital in which she was born because of bilateral swelling over the parotid glands noted on the fifth day of life. The infant had been born during the seventh month of pregnancy. Delivery was spontaneous but uncontrolled and unsterile. Birth weight was 3 pounds 9 ounces. Respirations were not immediately established and a three-minute period of resuscitation was necessary. She had always been in rather poor condition and did not suck well. Her rectal temperature had never risen above 95°F. Complete blood count performed on the fifth day of life revealed a hemoglobin of 22.9 gm. per 100 ml., hematocrit of 66 per cent and a total white cell count of 19,500 per cu. mm. with a differential count of 36 segmented neutrophils, 38 band form, 7 metamyelocytes, 17 lymphocytes, and 2 monocytes.

When admitted to Children's Hospital she appeared to be acutely ill, was slightly jaundiced, and was having irregular respiratory movements with periods of apnea. Rectal temperature was 95°F., and the heart rate was 140 per minute. There were hard swellings of the parotid regions, extending from the ear lobe to below the angle of the mandible bilaterally. The skin overlying these swellings was erythematous. The openings of Stensen's ducts were not visualized. The remainder of the physical examination was non-contributory.

Over the following two day period intensive therapy was instituted. She received intravenous fluids, chloramphenicol intravenously, and penicillin intramuscularly. Despite therapy her condition steadily worsened and she died two days following transfer, on the seventh day of life.

DISCUSSION

Dr. Guin:

At postmortem examination the infant appeared to be a poorly nourished 3½ pound negro girl with easily discernible bilateral swelling in the parotid regions. The skin overlying the parotid glands was incised, following which each gland collapsed under pressure with the escape of necrotic yellow material. The lungs were markedly engorged and on microscopic examination exhibited mostly focal hemorrhage with very little inflammatory reaction. Pathological changes in the remainder of the body organs were insignificant. Microscopic examination of the parotid glands showed almost total destruction of each gland. The only remaining glandular tissue was quite hemorrhagic and necrotic; only a few scattered salivary alveoli could be identified. Masses of bacteria were observed in the necrotic material. Culture of this material grew *Staphylococcus albus* and *aureus*. Culture of the heart blood was sterile.

Dr. Jackson:

This case is very interesting from two points of view. First from the viewpoint of how fetuses and newborn infants contract infection, and second, from the standpoint of the antibiotic resistant staphylococcus now plaguing hospitals from one coast to the other.

I would like to review briefly the obstetrical history of the mother of the infant. She was between her thirty-first and thirty-second week of pregnancy when she came into the emergency room after three hours of labor. Five minutes after she arrived her membranes ruptured spontaneously and five minutes later she delivered her baby. She consequently had a total labor of three hours and ten minutes.

Now, to be sure, birth was uncontrolled and "undraped" as we say, but these babies usually do fairly well. An important thing to consider in the history is the difficulty in resuscitation of this baby. Her pharynx was aspirated in the emergency room and she was given oxygen there. In the delivery rooms the aspirators are autoclaved, covered with gauze, and an attempt made to keep them sterile. No such an attempt is made in the emergency room as far as I can determine. The course of the baby has been previously described, essentially a downhill one, unmodified by therapy. Incidentally, mouth cultures taken before she was transferred to Children's Hospital grew hemolytic *Staphylococcus aureus* and *Escherichia coli*. The staphylococcus was resistant to all antibiotics and sulfonamides.

How does infection in a fetus or newborn develop? As you all know, infection may occur at one of three times. The fetus may contract infection prior to the onset of labor, in the intrapartum period, or in the postpartum or neonatal period. In order for infection to occur in the antepartum period it is necessary for the organism to cross the placental barrier. Viruses, of course, are able to do this; there are many well authenticated cases of viral infection with onset in the antenatal period. Recently it has also been felt that in mothers with bacteremia it is possible for bacteria to pass from the maternal blood into the chorionic villi and then into the fetus. However, there is nothing in the history of the pregnancy to suggest that the mother had septicemia.

During the intrapartum period, transmission of the infection is usually due to ascending infection in the reproductive tract or by aspiration of organisms from the vagina. Organisms have been cultured from the amniotic fluid of mothers six hours after the onset of labor even in the presence of intact membranes. Once membranes have ruptured the organism can be cultured from the uterus in a much shorter time. This mother, however, was in labor for only three hours and ten minutes and her membranes did not rupture until five minutes before delivery. Staphylococci are normal components of the vaginal flora of most women and just as with thrush, a fetus can aspirate a staphylococcus in passing through the vagina.

Lastly we have to mention contamination in the postpartum period. This, of course, raises the entire question of infections from antibiotic resistant staphylococci being reported in hospitals all over the country. These staphylococci have been cultured from all sorts of places in the hospitals. They have been cultured from bed linen and they have even been cultured from soap containers in operating rooms, presumably a cause of some postoperative infections. They may also be cultured from the nasopharynges of hospital personnel. The question of an unsterile aspirator remains an important one in this case. Additional factors may occur in the nursery when even though nipples and bottles are autoclaved they are allowed to sit around. Any of the foregoing seems to be a likely source of infection.

Dr. Ross:

There are a couple of things which I would like to say in regard to the problem of *Staphylococcus aureus*, both as it obtains in the hospital population and in the population at large. We know that a good many people carry staphylococcus in their oropharynges at one time or another. In a group which has been in a hospital over a prolonged period the incidence of staphylococcus carriers might range anywhere from 50 to 80 per cent. I do think it is important, however, to point out that the mere isolation of *Staph. aureus* from a throat or from an operative site does not necessarily constitute *a priori* evidence that the patient is suffering from a staphylococcal infection. Because of the ubiquitous nature of *Staph. aureus*, on our hands, in our nares, on the bed linens, on floors, in the air, the mere isolation of the organism does not indicate infection. All too frequently, for example, a diagnosis of staphylococcal pneumonia is based only on the fact that an organism has been isolated from the oropharynx. One cannot generally assume that the organism isolated in the upper respiratory tract is responsible for the lower respiratory tract infection and this is particularly true in the case of staphylococcus. Similarly, isolating staphylococcus from an open wound does not necessarily constitute a cause and effect relationship. The only way we can be sure that staphylococcus is the causative agent of the surgical infection in question is to isolate it from a closed lesion where there is no external drainage as in an abscess, and even there great care must be taken following incision and drainage not to contaminate the swab when taking the culture. Of course, the best way of being certain is by isolation of the organism from the blood stream. However, one must include an admonition to interpret bacteriology reports with care in view of the frequency of blood cultures contaminated with *Staph. aureus*.

Another important factor to consider is that most of the recent work done on the staphylococcal resistance problem has been on *healthy carriers*. The demonstration that staphylococci may be quite resistant to antibiotics is *not* predicated on work done on patients with disease due to *Staph.*

aureus. Another common fallacy is that a staphylococcus susceptible to an antibiotic may show increasing resistance while the drug is being given to the patient. That is not true. A staphylococcus, initially drug sensitive *will not* generally become resistant during the course of therapy.

As previously pointed out by Dr. Jackson, most hospital personnel have been shown to be carriers of staphylococci, extremely resistant to most antibiotics currently in use. However, the general population does not share this same high incidence of resistant staphylococci. Only 10 to 18 per cent of non-hospital staphylococci have been found to be penicillin resistant. This contrasts with the hospital population where the incidence of penicillin resistant strains is about 80 per cent; similarly about 45 to 55 per cent of hospital strains are resistant to the tetracyclines and 15 to 20 per cent resistant to erythromycin.

I wonder how different the problem is today from what it was, say 15 or 20 years ago, before the advent of antibiotics. We do know in perusing the literature that staphylococci were as plentiful then as now. There really is not convincing evidence that the virulence of staphylococci has been enhanced by the advent of antibiotics. I think it is fair to say that the incidence of staphylococcal disease in hospitals is greater now than it was then. This is primarily due to the replacement of antibiotic susceptible staphylococci which the patient may have when he enters the hospital by antibiotic resistant strains which he picks up in the hospital. I think a point worthy of mention is that some people are persistent carriers of staphylococci and some are not. This applies to people who have never been hospitalized as well as to those who have. The reason for this difference is not known at the present time.

What can we do about the antibiotic resistant staphylococci which we find in the hospital. Dr. Jackson has indicated that many "sterile" instruments or solutions are quite contaminated with staphylococci, if we were to take the trouble to culture them. There is no simple answer to the problem. The organism is so widespread that it is almost impossible to eradicate it from any hospital. We can invoke some measures which might help cut down the incidence of cross infection. One can use more careful techniques when doing a venipuncture and take more precautions with subcutaneous infusions. We have all seen abscesses resulting from the administration of clyses which I am sure could have been avoided had more care been employed. Perhaps we need a return to the old Listerian principles of antisepsis, and a more concerted effort on the part of the medical, surgical, nursing and housekeeping staffs of the hospital to tighten our defenses against staphylococcal cross infection on the wards. Dr. Rountree of Australia has used a bacitracin neomycin combination incorporated in a nasal jelly and instilled it in the nares of hospital personnel. She reports

that by so doing the incidence of nasal carriers of the staphylococci has been substantially decreased. I think this is an area that needs further investigation, however.

The use of antibiotics in treatment of these resistant staphylococci deserves special comment. Antibiotics which are most useful in the treatment of these strains include erythromycin, chloramphenicol and novobiocin. These drugs thus far have not shown a substantial increase in percentage of resistant strains of staphylococci. This may be transitory, however, since staphylococci have in the past shown the distressing penchant of developing drug resistant strains over a period of time.

INTRACRANIAL CALCIFICATIONS

Diagnostic X-Ray Brief

Isidore Lattman, M.D.*
Joseph M. LoPresti, M.D.†

The presence of intracranial calcifications poses a number of problems for the roentgenologist. He must, first of all, be familiar with the normal, physiologic occurrence of such calcifications, e.g., the pineal gland and choroid plexuses (Figure 1). The anatomical location of these structures facilitates this interpretation. In addition, artifacts, such as curls of hair, and islands of bone in the calvarium must be differentiated from intracranial calcifications. Secondly, he must have a knowledge of the heterogeneous groups of disease processes which can produce ectopic calcifications within the cranium. The differential diagnosis is long and difficult and the interpretation must depend on:

1. The location of the lesions, e.g., the calcification of a craniopharyngioma is located in the suprasellar region; hyperparathyroidism produces calcification of the basal ganglia.

2. The age of the patient, e.g., toxoplasmosis is more apt to occur in the congenital form in infants (Figure 2).

3. The appearance of the calcification, e.g., calcific deposits in cerebral hemangiomas will occur in the blood vessel walls and produce a "worm-like" pattern.

4. The presence of skin lesions in the patient, e.g., adenoma sebaceum

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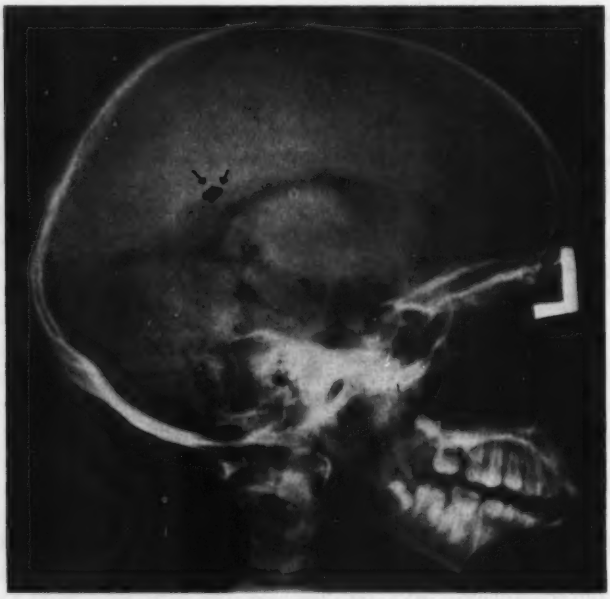

FIG. 1. Pneumoencephalogram of skull in lateral view showing an intracranial calcification (Retouched). This represents a physiological calcification of the choroid plexus.

of the face in tuberous sclerosis or a nevus flammeus of the face in the Sturge-Weber syndrome.

5. The associated signs of increased intracranial pressure makes a brain tumor more likely.

6. Blood chemistries and other laboratory observations are sometimes helpful.

Finally, the radiologist must be cognizant of the newer additions to the list of diseases which may cause intracranial calcifications. An example of this is cytomegalic inclusion cell disease of the newborn.

As indicated, the differential diagnosis is complex and the causes may be divided into physiologic and pathologic:

1. Physiologic
   a. The choroid plexuses
   b. The interclinoid ligaments
   c. The petroclinoid ligaments
   d. The falx cerebri
   e. The pineal body

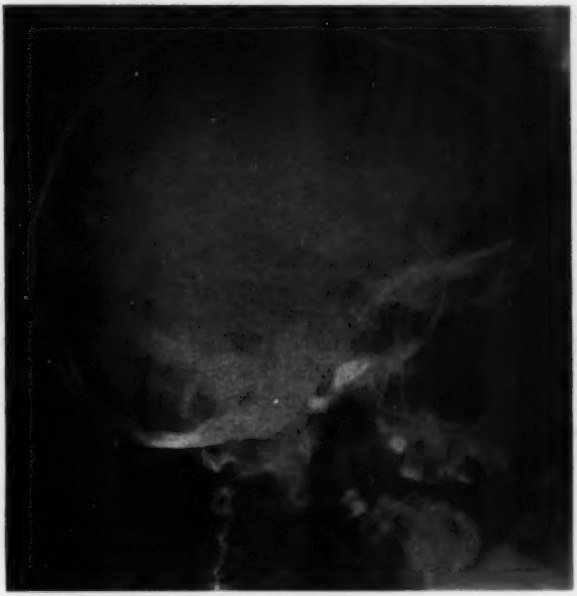

FIG. 2. Lateral view of the skull showing disseminated areas of intracranial calcification. This was thought to represent a healed toxoplasmosis.

f. The Pacchionian granulations
2. Pathologic
   a. Neoplastic
      1. Craniopharyngiomas
      2. Ependymomas
      3. Gliomas
      4. Intracranial teratomas
      5. Lipoma of the corpus callosum
   b. Inflammatory
      1. Old cerebral abscess
      2. Tuberculomas
      3. Cysts due to cysticercus, echinococcus, trichina
      4. Toxoplasmosis
      5. Torular meningo-encephalitis
      6. Primary coccidioidal meningitis
      7. Cytomegalic inclusion disease
   c. Vascular
      1. Sturge-Weber Syndrome (Cerebral Hemangioma)

2. Tuberous sclerosis (Bourneville-Pringle Syndrome)
3. Lindau's Syndrome

d. Traumatic
1. Cephalohematoma
2. Subdural hematoma
3. Intracranial hemorrhage

e. Endocrine
1. Hyperparathyroidism
2. Hypoparathyroidism
3. Pseudohypoparathyroidism

All of the preceding factors must be evaluated before a diagnosis is made. Frequently, no clue as to the accurate diagnosis is present in the skull x-rays. The practitioner then is faced with the problem of establishing a definitive etiology. This may involve viral studies or expensive serologic tests. On occasion, the radiologist may prevent needless worry or expense by accurate interpretation.

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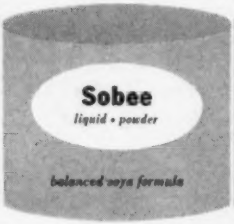

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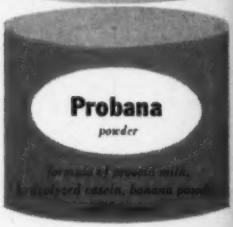

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